1990/871P

THE HIGH COURT

UNITED STATES TOBACCO (IRELAND) LIMITED

AND

UNITED STATES TOBACCO, INC: Plaintiff

IRELAND, THE MINISTER FOR HEALTH

AND

THE ATTORNEY GENERAL: Defendants

ACTION HEARD BEFORE MR. JUSTICE BLAYNEY

IN DUBLIN ON NOVEMBER 27, 1990, AND FOLLOWING DAYS

TRANSCRIPT OF EVIDENCE ON NOVEMBER 29, 1990:

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I hereby certify the following to be a true and accurate transcript of my shorthand notes of the evidence in the above-named Action.

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BERNARD EUGENE McCARTAN, HAVING BEEN SWORN, WAS EXAMINED AS FOLLOWS BY MR. GLEESON:

346 Q. Mr. McCartan, I think you were born in Belfast on the 5th of November 1944?

A. That is correct.

347 Q. And you are a Bachelor of Dental Surgery from Queen's University in 1966, a Fellow in Dental Surgery, the Royal College of Physicians and Surgeons of Glasgow 1975?

A. Yes.

348 Q. And a Fellow of the Faculty of Dentistry, the Royal College of Surgeons of Ireland, 1989.

A. That is correct.

349 Q. A Master in Dental Science in Dublin 1990 and also you hold an M.A., Dublin?

A. Yes.

350 Q. You are the Senior Lecturer in Oral Medicine in the School of Dental Science Trinity College Dublin since 1978 and the Head of the Department of Oral Medicine and Pathology.

A. Yes.

351 Q. And you're a Consultant in Oral Medicine in the Dublin Dental Hospital since 1975 and Head of the Division of Oral Surgery, Oral Medicine and Oral Pathology?

A. Yes.

352 Q. And you are a Consultant in Oral Medicine in the City of Dublin Skin and Cancer Hospital, Hume Street Hospital, since 1981?

A. Yes.

353 Q. You are a member of the Dental Council on behalf of the University of Dublin?

A. Yes.

354 Q. And that is the statutory body governing dentists in Ireland?

A. Yes.

355 Q. And also a member of the Fitness to Practice Committee of that council?

A. Yes.

356 Q. And a member of the Scientific Committee?

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A. Yes.

357 Q. And you are an examiner in the Dental Fellowship Examinations of the Royal College of Surgeons in Ireland and the Royal College of Physicians and Surgeons of Glasgow?

A. Yes.

358 Q. I think you are also the single holder of an academic or hospital position in Ireland which is designated for oral medicine?

A. So I understand.

359 Q. Could you just outline in layman's terms the sort of work you do?

A. I deal, My Lord, with diseases of the soft tissues of the mouth other than diseases of the gum, and I deal with the oral manifestations of the diseases elsewhere in the body.

360 Q. What does your work actually comprise?

A. it ranges from mouth ulcers through a variety of conditions, some of which are shared with skin diseases, through to cancer.

361 Q. Do you deal with pre-malignant conditions in the mouth?

A. I do.

362 Q. What would they be?

A. There are a number of pre-malignant diseases which include leukoplakia, but there are others like lichens planus.

363 Q. Can you come to the way in which people come to be referred to you -

A. Many people come to me for a variety of causes. I think the largest group comes from general practitioners and dentists. Another large group would come from general medical practitioners. Some would come from fellow dental specialists and some from medical specialists. Mostly they are dermatologists and gastrointerologists.

364 Q. So far as the dermatologists are concerned, you might be regarded as a sub-specialist of their field.

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A. Yes, except that I haven't medical qualifications or training in dermatology.

365 Q. Yes, but you are concerned with the skin inside the mouth. Could you tell us about leukoplakia?

A. Leukoplakia is an oral lesion which has an international agreed established definition by the World Health Organisation, and that definition is essentially of any white piece or plaque which can neither clinically nor pathologically be designed as any other disease. It is a definition almost by exclusion.

366 Q. A residuary definition?

A. Yes. The generally accepted view is that approximately three to six percent of all leukoplakia will become malignant - that is cancer. And some studies which have carried out longer periods of observance have shown perhaps higher incidents of malignant transformation.

367 Q. How high?

A. I have no recent papers. I think we're talking about the recent, 40%. I'm not absolutely sure on that. There are probably, I think, papers pre-dating the '70's.

368 Q. Are you familiar with oral cancer?

A. I am, yes.

369 Q. Is it an unpleasant condition?

A. It is an extremely unpleasant condition.

370 Q. Tell us something about it?

A. Well, oral cancer usually you see first as an ulcer in the mouth which fails to heal. The ulcer, if not treated, gradually erodes the tissues underneath. It will spread to the underlying bone and it may spread to the outer surface. Eventually, it will spread from its primary sites to other sites in the body brought by the blood stream and through the lymphatics. And the majority of people with cancer of the mouth will die from that. I cannot give you accurate Irish figures. I can only conjecture on figures in my hand, that approximately 80% of the people in Ireland with [illegible], they die from it.

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371 Q. I think you have for some time past kept a personal record of the smoking or tobacco use habits of people that are referred to you?

A. Indeed, since I overcame my own habit.

372 Q. When was that?

A. That was approximately five and a half years ago. I informally kept a record at first. I had noted tobacco usage. And, after I stopped smoking myself, I asked most of my patients about smoking and I have it filed and I now have a box which you cannot ignore which has to have an entry, and, for the majority of people, I make a record of tobacco usage.

373 Q. I think your patients come from the whole of Ireland, apart from Cork and Kerry?

A. Yes. Occasionally from the north of Ireland as well.

374 Q. About how many people of this population that have smoking habits come to you -

A. Unfortunately, the Dental Hospital does not keep accurate figures. I would think approximately 5,000 people.

375 Q. How many of those have admitted to you of their use of smokeless tobacco?

A. None.

376 Q. Are you familiar with the state of scientific knowledge in relation to the use of oral smokeless tobacco or part of it.

A. Part of it. It has not been a major problem in Ireland, therefore, it is not something I have kept abreast of constantly.

377 Q. Do you have a view as to the role of smokeless tobacco in relation to the health of the mouth?

A. I believe there is an overwhelming body of opinion which associates the use of smokeless tobacco in both European societies and Asian societies with a development of cancer in the mouth.

378 Q. How would you characterise the suggested association of the cancer in the mouth and the use of oral smokeless tobacco?

A. I don't quite follow.

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379 Q. What level of confidence have you in any connection -
MR. FITZSIMONS: The witness has been very fair and straight. He said he is of the view that there is an overwhelming body of opinion that there is an association. In other words, he is not putting forward any view on behalf of himself.

380 Q. MR. GLEESON: That is a fair objection. What is your estimate - bearing in mind your fairness - your view of the state of the literature as to the connection?
MR. FITZSIMONS: Has he read the literature first of all?

A. I can't use the term "Confident" in the statistical sense, but there is a very strong association and that oral cancer with smokeless tobacco arises in some cases to fifty times as high -

381 Q. MR. GLEESON: I think you have a personal interest in statistics?

A. I'm undertaking a post graduate diploma in statistics in University College Dublin.

382 Q. And you have an interest in statistics?

A. I have.

383 Q. What are the factors that have been identified, for example, in the United States as being material in the connection between the use of these products and oral cancer?

A. The first major point is that, unlike cigarette smoking, there is a site specificity: cigarette smoke goes down...but smokeless tobaccos are held in a particular site, and one finds lesions in those sites, and they are very specific. They tend to be leukoplakia though other lesions can be found. So, there is a site specificity and a lesion specificity.

384 Q. What inferences are to be drawn from those two specificities?

A. That it is very hard to deny an association between them.

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385 Q. What about duration or use of the pellets or Bandits or whatever you wish to call them?

A. The evidence on duration of use - one has several points: first of all, the number of years it is used. There is some evidence that the risks increase greatly with the number of years. There is also the evidence that the risks increase with the number of hours per day in which smokeless tobacco is held in contact. There is a problem in relation to the individual's items of tobacco used because, for example, one does not know with any individual how long the smokeless tobacco is held in place. So, an individual who uses smokeless tobacco doses may be using one or four doses in a certain time and another may use four doses in fifteen minutes... There is certainly one recent study from the Indian sub-continent which would suggest that there is a clear relationship with the number of items of smokeless tobacco used, the length of time for which each one is used and the number of years over which it has been used.

386 Q. Is there any difference involved as between male and female use of this pattern?

A. Again, in the Indian sub-continent, it is largely males who have the higher risks. And that seems to be associated with the use of chewing tobaccos. In Scandinavia, the use of smokeless tobacco by women appears to be uncommon and the hazards of lesions is equally uncommon, whereas in the southern United States - largely amongst that population which is of poor emigrants from these islands several hundred years ago - it is very heavily a custom amongst women, and the rates of oral cancer amongst women there are very high.

WITNESS WAS CROSS-EXAMINED AS FOLLOWS BY MR. FITZSIMONS:

387 Q. Doctor, your various comments about the Indian sub-continent and Sweden and the United States, do I gather they are not take from your own experience but from a, you have read some of the literature?

A. Yes, I have no direct personal experience.

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388 Q. Just to establish that for the record in case there was any doubt. You yourself have engaged in research - isn't that right - and you have written various papers for various journals?

A. I have very little published work.

389 Q. You have published quite a number of publications in dental journals.

A. They are largely extracts.

390 Q. But none of them deal with leukoplakia or oral cancer?

A. No.

391 Q. Or any of the matters we are concerned with here?

A. No.

392 Q. None of them deal with periodontal diseases other than lichens planus. That seems to be an interest of yours.

A. Periodontals is not an interest of mine.

393 Q. Lichens -

A. Yes, lichens planus is.

394 Q. And the connection between stress and oral disease - is there an association?

A. It is probably mechanically associated through people chewing their lips if they are under stress.

395 Q. Of course, there is no question of lichens planus being connected with the use of smokeless tobacco?

A. No. It is a separate pre-malignant problem.

396 Q. Do I gather you have read some of the epidemiological studies?

A. I have.

397 Q. How many of them?

A. I have read a number over the years. Recently I have read, I suppose, thirty or forty.

398 Q. I suppose preparing for this case?

A. Preparing for this case.

399 Q. Before that, you didn't have a knowledge of the subject?

A. No - No, I have had some interest in the subject since 1985 when one of my students, who was a United States citizen, imported some of these smokeless tobaccos,

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and the literature, I have kept an eye on it since then.

400 Q. So you have been reading since 1985?

A. I have been reading sporadically since 1985.

401 Q. Recently, how many studies have you read?

A. I couldn't give an answer to that.

402 Q. Two?

A. Eight or ten, I would think probably.

403 Q. You mentioned one study which said there was a very strong association, rising to 50 in one case - which study was that?

A. That was the study, the Winn study.

404 Q. Have you considered the I.A.R.C. ?

A. I have looked at the Surgeon General's report.

405 Q. It relies on the Winn study?

A. Yes.

406 Q. And, the 1986 Surgeon General's report expresses the view as a result of the view that smokeless tobacco is a causative cause of smokeless tobacco (sic).

A. Yes.

407 Q. Which is quite different from the 1982 report which simply says that it was a possible factor?

A. Yes. I haven't read the 1982.... I have simply heard what was stated to me.

408 Q. So, there was a change in the meantime it appears?

A. There would seem to have been a change.

409 Q. The Winn report is the one you would agree that is the most prominent of all these epidemiological studies?

A. It appears to be.

410 Q. And is the one most frequently relied upon by anti-tobacco advocates?

A. Yes, in relation to usage in the United States and Europe.

411 Q. And Miss Winn was certainly attached to the team in the I.A.R.C. contention, the team that produced the I.A.R.C. study. She is named. You know nothing about it?

A. I know nothing about it.

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412 Q. I think, as far as you go, you have been very fair. You said that, in your view, there is an overwhelming body of opinion that associated smokeless tobacco with oral cancer. What you are saying really is that there are a lot of opinions to that effect but you have not seen other opinions?

A. I have read some papers which have been noted as giving other opinions, but I am not sure they are necessarily contrary. I have read so many papers in recent days that I would be reluctant -

413 Q. There were papers, I take it, provided by the Department of Health? That you were directed to that source?

A. The only paper I was given by the Department of Health was an unpublished manuscript. Otherwise, all that I have read was published and through the libraries -

414 Q. And your conclusion is that there is a very strong association -

A. According to the study, there is an overwhelming body of opinion that associates them.

415 Q. So, you are not prepared to go as far as the last witness in his very strong statement on the tobacco?

A. I am not an epidemiologist. I do not know at which point in the practice of epidemiology one talks of causation.

416 Q. If you are going to express an opinion on the topic, you would approach the topic with care?

A. I would hope so.

417 Q. And you are not coming to the witness box as an anti-tobacco advocate?

A. No. I have very strong views on tobacco but I am not coming here as an anti-tobacco advocate.

418 Q. As the Winn study was shown to be methodologically defective, I take it that would be a reason for you to review the view you have taken of the literature?

A. Yes, except that I can say that I have seen one other reference and that the Winn study is very well done compared to other studies.

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419 Q. If it were methodologically defective, you would have to review the view you have taken of the assembled literature?

A. I would have to see what effect that would have on the study.

420 Q. In relation to the study itself - there seems to be an equivalent number of epidemiological studies for and against the proposition that there is an association between smokeless tobacco and oral cancer?

A. That is your statement and not mine.

421 Q. It is a fact.

MR. GLEESON: It is not accepted at all.

422 Q. MR. FITZSIMONS: These are the studies on smokeless tobaccos. Epidemiologically, there is a report saying "No association" and "an association". I think those reports should be up there. Are you familiar with these studies? Did you read the ones that didn't show an association?

A. I have read several of them, I think only two of them. I have also looked at the comments made on them in the Surgeon General's report.

423 Q. You have read two of them anyhow?

A. Yes.

424 Q. Dr. Wynder, who appears twice in this list, I am instructed is the first person who reported an association between cancer and tobacco in the fifties?

A. I also thought it was Richard Doyle (?).

425 Q. Firstly, maybe you're not in a position to deal with this because you said there was no smokeless tobacco in Ireland and you have not investigated any cases yourself?

A. No.

426 Q. But I think you can confirm at the very least that the reports indicate that smokeless tobacco does not cause periodontal and gingival diseases, damage to the salivary glands?

A. These periodontal and gingival diseases is an area I have no interest in whatsoever and I can't comment.

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427 Q. In relation to leukoplakia, there are many possible causes for leukoplakia?

A. There are not many. There is a list of causes but it is not a limitless list.

428 Q. What are they?

A. Nutrient deficiency, syphilis, ingestion of candida - which is a yeast - friction, alcohol, smoking. And I may have left one out. I think I have covered them essentially.

429 Q. So, if someone comes into you with leukoplakia, you will not know from the sight of it what caused it?

A. One can tell a certain amount by site and distribution. If there is in their cheek a lesion which is a shape...or I'm expecting a moving tooth and I would say that that is because of friction. I can contemplate smoking, and then leukoplakia may go away.

430 Q. You didn't, of course, come across a case of passive smoking that can cause this condition?

A. NO, I don't see how passive smoking could. I would suspect that the leukoplakia association with smoking is due to distillation of hot tars in the mouth, and a smoking room air wouldn't do that to the mouth.

431 Q. Passive smoking is an alleged danger in our society now?

A. Yes, but I have never heard it to cause oral cancer.

432 Q. Sticking with leukoplakia for the moment, doctor, - just to put a number of general propositions to you: you would agree with the first proposition that leukoplakia is one that is found on clinical examination.

A. To make a true diagnosis of leukoplakia it requires a biopsy as well to exclude other causes. This is not always done.

433 Q. But the condition is such that it doesn't provide information about the pathological or observed condition other than in the way you have described?

A. Except that certain pathological changes are found in leukoplakia.

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434 Q. And I think you have indicated from the list of factors - whether or not smokeless tobaccos are a factor - there are many other possible causes in each case?

A. Yes, there are. One would assume that a good research paper would look for these and go into it.

435 Q. I put to you that most smokeless tobacco users, they don't develop leukoplakia, that there is a research - ?

A. There is a study published this year which suggested 214 out of 423 American professional sportsmen had leukoplakia at the time of examination. I understand this work was carried out in the spring of 1988.

436 Q. I don't follow. What is the implication of that?

A. That 50% had it. Whether that is the most or not the most, I cannot comment.

437 Q. Did they take into account the nutrient factor? I imagine that American sportsmen or footballers would be inclined to take an odd beer in the least?

A. Yes.

438 Q. Did it take into account other factors?

A. It tended to take into account the use of cigarettes, but it didn't take into account these other factors.

439 Q. Baseball players are generally older in that they carry on until their 40's and 50's.

A. 70% of the people they examined were between 20? and 29.

440 Q. One would expect that they are consumers of alcohol?

A. I think that is reasonable to assume.

441 Q. But the study didn't take account of the possibility of alcohol being a factor?

A. No.

442 Q. So, the study is methodologically defective?

A. I would have to comment on that I am not aware of any study which showed alcohol, which would show leukoplakia anywhere at 50%. Also, if it was to be a correct matter, it would have to be a minor one.

443 Q. What about nutrition?

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A. I don't think we're talking about under nourished people here.

444 Q. Baseball players -

A. I would be very surprised.

445 Q. Did the study take account of the other factors you mentioned?

A. It attended to show control for oral hygiene and show control for alcohol.

446 Q. I thought you said it didn't?

A. I'm not sure in what way they did that. They made some attempt for alcohol.

447 Q. It sounds like a very sloppy study?

A. I don't know. I'm not an epidemiologist. I know the people who carried out the study are the reputable people.

448 Q. I'm instructed that the people who carried out these studies that showed no association between smokeless tobacco and oral cancer were very reputable people with international reputations in some cases.

A. Yes. The title of this document concerns me slightly. I think there is a difference between reporting no association and not reporting an association. I think a statistician would want to make a distinction between these two. And I'm not sure which of these categories this falls into.

449 Q. No association -.

MR. JUSTICE BLAYNEY: Can you deal with the question the witness is facing, that there is a very clear difference between not reporting an association and possibly reporting no association.

MR. FITZSIMONS: The distinction is as simple as that.

MR. JUSTICE BLAYNEY: Yes, but can you say in the title what is correct and whether it includes reports which didn't report an association as distinct from reporting no association?

MR. FITZSIMONS: These are studies that considered the question of a list of smokeless tobaccos and oral cancer and the result reported no association between the two.

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MR. JUSTICE BLAYNEY: So, you are saying that definitely there is no question of any of these reports not reporting any association?

MR. FITZSIMONS: They reported no association. I take Your Lordship's point. It was a test with a particular objective, to test a possible link between the two. The results reported no association. The conclusions, in consequence, were that there was no association. I think it is basically the same thing again.

MR. JUSTICE BLAYNEY: Well, I don't think it is the same thing. It is a distinction between not reporting any association and reporting positively there is no association.

MR. FITZSIMONS: All they can do is give a statistical result. They don't give a conclusion. Some one has to look at these statistics that come from the survey carried out and express a view on those statistics.

MR. JUSTICE BLAYNEY: Well then, is this title correct, because this seems to be reporting a conclusion? In other words, you say that, in regard to some, they reported no association? Now, that is clearly reporting a conclusion -

MR. FITZSIMONS: I take Your Lordship's point. If it is incorrect, the study in the other list is similarly incorrect - the epidemiological studies report an association between tobaccos and oral cancer.

MR. JUSTICE BLAYNEY: I know.

MR. FITZSIMONS: To that extent, if there is any ambiguity about it, both titles are ambiguous. All that an epidemiological study can do is produce statistics and to have a view it has to be taken as the compilation of those statistics. In relation to one list of the study, it is reporting the association. The statistics showed up when evalued as indicating a link between the two, vice versa with the other list.

MR. JUSTICE BLAYNEY: And the vice versa would mean not indicating a link rather than indicating no link?

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450 Q. MR. FITZSIMONS: That is correct. Coming to the baseball report, who were the authors of that?

A. The authors were Green, Daniels, Silverman...there were various people involved in dermatology and so on in San Francisco.

451 Q. Is there a Connolly suggested in the list?

A. No.

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Q452 Can I put it to you, Doctor, that the relationship between oral leukoplakia and oral cancer is unknown.

A Do you mean the epidemiological relationship or the carcinogenic relationship?

Q453 Yes. Well, sorry about that. I think we have established that medical science does not yet know the pathogenesis of cancer, in other words, the mechanisms as to how cancer is caused. I remember putting it to you in that context, the link between it is not known?

A No. Pathogenesis is not my field of expertise, but I understand a number of suggestions have been made why alcohol, why cigarette tar, why smokeless tobacco might cause cancer, but none of these are definitively proved.

Q454 Yes, of course, and I put to you a proposition that persons with leukoplakia who do not use tobacco develop oral cancer more frequently than persons with leukoplakia who do use tobacco, results of several studies apparently?

A That I am not familiar with. That surprises me, My Lord.

Q455 Well, I can produce four studies that lead to, point to that direction?

A I'd need to examine them and see what populations they were done in.

Q456 I mean, I will produce them but I won't have the time to engage in -. You mentioned, in relation to tobacco, that you had an interest having given up cigarette smoking, do you note as to whether or not the patients use tobacco. I take it you do the same thing with alcohol?

A I do, yes. Can I correct that answer. I enquire about the use of spirits, not the use of beer and wine.

Q457 Doesn't beer contain nitrosamines which these reports go into great detail alleging because they are part of smokeless tobacco therefore smokeless tobacco is --

A I understand nitrosamines are contained in a lot of food stuffs. It's a question of the level of nitrosamines within them.

Q458 The IARC report, I am instructed, makes no distinction between beer, wines and spirits, in discussing a link between oral cancer and alcohol?

A Certainly the studies with which I have been familiar until now have concentrated on spirits, particularly on badly distilled spirits.

Q459 Do you [illegible] many patients?

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A No patient is admitted to me from the use of illicit spirits.

Q460 Just a couple more questions, Doctor. Now, you did refer to an Indian study, I think it was a fairly recent Indian study, in the course of your evidence. Isn't that so?

A That is correct, yes.

Q461 Isn't it correct that in as far as that and other, I put it to you that in insofar as that and other Asian studies are concerned, that no useful conclusions can be drawn from them in view of the entirely different diets, diets and nutritional background and populations in those areas?

A There are certainly difficulties in drawing and conclusions from different studies, but when one sees the different studies which compared effects of chewing tobacco with chewing other substances alone and are mixed with tobacco and smoke in a variety of ways and when these are corrected for, chewing tobacco still seems to be associated with high oral cancer, then I think one can say that they are not that different in Indian --

Q462 I have to put it to you that the 1979 Surgeon General's report stated that the validity of applying the results of Asian studies to the United States is questionable because of differences in the type of tobacco chewed, nutritional states and social habits?

A There are a number of problems.

Q463 Page 13 to 39 of the 1979 report. Would you agree with that?

A I said there are problems, but when it comes to the same conclusion of reports taken in Europe and North America, I think it must be legitimately born in mind.

Q464 I take it, Doctor, you would agree, just to finish off, that one cannot regard the results of studies, epidemiological studies, investigations of various kinds in this and indeed equivalent areas, as being infallible?

A No, no statistical study can ever be infallible. One always has to set a confidence level.

Q465 And doctors and scientists always retain the right to change their minds?

A Yes.

Q466 And I take it you could give various examples of where medicine had taken up affirm view in a particular area but later on changed it's mind?

A I can think of examples from my own discipline.

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Q467 And whilst the view at the moment might be held very strongly that the very fact that it was held very strongly did not mean that due to the absence of knowledge it was the correct view?

A Again, I am not a epidemiologist, but I think there are occasions where large bodies of evidence have been overturned relating to evidence acquired, shall we say, in the prescientific era.

THE WITNESS WAS RE-EXAMINED AS FOLLOWS
BY MR. GLEESON:

Q468 Arrising out of my friends last question, the evidence we are talking about in this case, as I take it, in the scientific area, I won't ask you to fix the date of commencement of the scientific area, but this evidence is in the scientific era?

A In general the evidence that I would wish to look closely at would be evidence after 1979 which is when the World Health Organization recreated an international definition of leukoplakia and that, I think, would be in the scientific era.

Q469 And is it, in the language that we are speaking in now, is it a large body of evidence?

A I would regard it as very substantial body of evidence.

Q470 Just going back to the baseball players for the moment, I am not sure that you gave us, you gave us the figures of those with leukoplakia and those that hadn't. But did you say that they were all users of oral snuff or --

A The figures are, there were approximately eleven hundred players examined. Of those 493.

Q471 493?

A Were non-users of smokeless tobacco and 423 were recent users, which was defined as within the previous week.

Q472 423?

A And the results of leukoplakia instance were quite different between the two groups. In the first group there were 864, "93 had leukoplakia....." (quoted).

Q473 8 baseball players had leukoplakia.

A Yes, and 214 of 423 who had used it within the last week had leukoplakia and there was a close relationship.

Q474 Assuming, and it is a assumption, that that is a

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correct recording of those findings, let's say you had made those findings, that's a assumption I am going asking you to make, what interest would you draw personally as a scientist?

A Well, I haven't actually drawn up a statistical analysis of this but I think this is one of those cases where common sense would run well ahead of any statistical analysis, an instance of 2% in a group of 400 people versus 50% in another group, I think, is a very significant finding.

Q475 - percent in the non-users and 50 percent in the users?

A Yes.

Q476 I want to touch upon the mystery of cancer, the pathogenesis of carcinoma. You indicated to Mr. Fitzsimons that this is not fully understood. Are there plausible biological mechanisms to suggest the connection?

A Again this is not my field, but in the case of alcohol, both local and generalised mechanisms have been suggested including direct alteration to the lining of the mouth. In the case of smokeless tobaccos it's understood that nitrosamines have been associated particularly if those substances are altered while they are chewed in saliva.

Q477 Now, Mr. Fitzsimons asked you about the two schedules, which I call them, which were put in before lunch and I didn't raise those with you, but I am going to raise them in some detail now.

Firstly, in your view, does the list described as Epidemiological Studies Reporting An Association Between Smokeless Tobacco And Oral Cancer, is that a comprehensive list of epidemiological studies which make that report, or report an association, are they all the studies that say, yes, there is a connection?

A No, I don't think so. Certainly it excludes all studies which have occurred outside Europe and North America. I am not sure, I would need to --

Q478 Well, another witness will be able to list - - There are about ten there.

Now, I'd like you to look then at the other list and to consider the status of these documents. The first thing that may be observed is this, is that comparing the two lists, on the list where no association was reported, the first is Wynder, and he's also reported in the same year as reporting an association on the other list, in a different [illegible] will come to both of them in due course.

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Isn't that right. There is the Stockholm and the American report?

A That is right.

Q479 We will look at those reports. We don't know the author of these two schedules, but presumably the author is going to give evidence as Mr. Fitzsimons promised. Now, I think of the nine negative association --

MR. FITZSIMONS: I didn't promise anything.

MR. GLEESON: "There will be evidence" is the expression used.

MR. FITZSIMONS: These lists have been put in as a list of studies. The lists will be, I propose to ask my witnesses to go through them one by one. They are put in to assist the court. I can produce the individual studies and go through them one by one that way, if my friend wants, but this is the convenient way of doing it.

MR. GLEESON: I have no objection to the convenience of putting them in this format. Indeed it's helpful, but I am assuming, on foot of Mr. Fitzsimons statement that there will be evidence, that some witness will swear to the distinction.

MR. FITZSIMONS: Yes.

MR. GLEESON: And will assert that one list is one, a complete list within some definition of the, those that report an association and the other is a list of those that don't. That's what I am assuming and no more than that.

Q480 MR. GLEESON: Can you now take the Surgeon General's report and you may not have a copy there, do you? (Book landed to witness), and look at first, at page 12 of the introduction. That's Roman numeral 12 of the introductory part in which the contributors to the report are designated. There is a list, that goes on for a number of pages, of the learned people that worked on this project, I think, Mr. McCartan, is that right?

A Yes.

Q481 And I think on page 12 those who were contributors to Chapter 2 are listed and Chapter 2 is the chapter which deals with epidemiology and which lists of the negative schedule, if I can put it, the "no association" schedule, lists 8 of the 9 articles there, actually discusses 8 of the 9 articles, and gives a rather different impression. But before you turn to Chapter 2 I want you to read for the court, the list of expert contributors to Chapter 2 and then

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I will ask you a question of them, with their qualification. I know this is --

A This section is headed Carcinogenesis Associated With Tobacco Use. (quoted).

Q482 They are a serious and competent group of people to talk about the topic?

A It's a very weighty group of group of them to discuss it.

Q483 Can I ask you then to just to take a note of the, it may be convenient if you take the "no association". But I want to give you the foot note reference which is used in Chapter 2. Chapter 2 of the foot notes, you refer to each of these allegedly "no association" papers and I will give you them in order, Wynder et al, the foot note is 25. Peacock is 27, Martinez is 30, Smith 43, the next Smith, 44, Browne, 32, Wynder and Stellman, 34 and Winn et al, 42. I hope they are all right.

But can I ask you now to look at the Surgeon Generals report in Chapter 2 and let's look at the way in which the first of those reports, Wynder et al, that's at foot note 25, if I can ask you to go to foot note 25 at Chapter 2.

A On page 40?

Q484 Page 40.

A Page 40.

Q485 Yes. I think it starts Wynder et al..

A Perhaps I am looking at the, Oh,, sorry, I am looking at 35. I should be looking at 25. 25, Wynder, on page 36.

Q486 Now us just to check your reference first, if you go a few pages on in the book you will see that the reference is to the first of the studies on the "no list"?

A It's impossible to tell from the citation, but it appears to be.

Q487 But I think what's distinctive is it's the Swedish Wynder rather than the American Wynder. You see the list just says Wynder. But it does say Sweden as the place where the cases were taken and you will find that Wynders work in '57 was done in Sweden and the other was done in the States. So I think that's correct. Now can you just read what the Surgeon Generals report says there?

A "Wynder et al reported on....." (quoted).

Q488 Just stop there. Just take that sentance, "the author states that the data suggested that a threefold risk is associated with the duration of

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chewing of tobacco for cancers of gingiva and oral cavity". If that's a correct report of what the paper actually says, is that, in your view, properly described as an epidemiological study of reports of no association between smokeless tobacco other and oral cancer?

A No.

Q489 Perhaps you'd complete the reading of that paragraph?

A "in addition data were not adjusted....." (quoted).

Q490 Just pause there. That's the other Wynder, I think, that's put into the positive category. It doesn't matter, you needn't follow it up. "Tobacco chewing was found to be more common among men...." (quoted).

Now, if I can ask you now to move to the next paragraph because that is indeed a reference to the second of the "no association" journal references. There is a note indeed at the foot of page that turns it clearly into an association reference, but just read what the Surgeon General said first?

A "Peacock et al....." (quoted). Do you wish me to explain these terms?

Q491 No, it's not necessary.

A "And compare....." (quoted).

Q492 And table 2, I think, appears in the Surgeon General's report at the top of the page?

A That is correct.

Q493 "The overall", carry on in the report.

A "The overall....." (quoted).

Q494 Now can you tell us what the point zero indicates there?

A The 2.0 implies that if you compare the absolute risk of the patients and the control group developing oral cancer, it was twice the group being studied.

Q495 In laymans terms, there was double the risk?

A Double the risk.

Q496 In the group who were users?

A Yes.

Q497 And it tended to be, as the note at the foot of the "no schedule" says, that the association was largely in the older men, which is, of course, where you would expect it to be because people, the more you use the product the more likely you are to get cancer?

A Yes.

Q498 Would you describe the Peacock study as appropriate to a list with anyone adopting even the level of scientific rigidity that you'd expect from a [illegible] student to be properly described as

http://legacy.library.ucsf.edu/tid/ouf87a90/pdf Document Lorillard Industries et al. v. Engle et al. No. 94-08273

a study reporting no association between smokeless tobacco and oral cancer?

A No, I think the correct interpretation is, if you can refer to the 1990 conference, that includes in fact the value for the chrome group which is one, "Reference Chrome" and one would have to say that they have failed to prove an association but one could not go and say that there is no association. That would be a difficult step to take.

Q499 Now, if we go to Martinez then, and that's footnote 30 in the Surgeon General's report. I think it's three paragraphs on, if I am not mistaken?

A Page 39.

Q500 Martinez?

A "Martinez reported on...." (Quoted).

Q501 Can I just stop you there. In laymans terms does that mean that the risk of catching oral cancer was 11.9 times for chewers as opposed to non-chewers and a - pharyngeal of 8.7?

A The figure for pharyngeal is the not stastically significant but for oral cancer it also falls within the confidence interval therefore the association is not proven.

Q502 And what is the, what is the reference then to the relative risks is, what is the worth of reference to relative risks in that context?

A It's the, I suppose it's the kind of figure which makes you say it is worth looking at these things a lot further, there seems to be something here.

Q503 A suggestion in what direction?

A A suggestion in the direction of an association.

Q504 And if you just read the last sentance then?

A "These numbers do not include the experience...." (quoted).

Q505 When you say not proven in the previous sentence, you mean not proven in the statistical sense?

A Yes.

Q506 Now, move quickly, if we can, to Smith which is 43, I think it's about 5 or 6 paragraphs on from there. It's in cohort studies, I think. Yes, the second paragraph under cohort studies. That's forward a little bit ?

A Yes.

Q507 This is a reference to the forth of the papers on the plaintiffs list, the forth and the fifth, yes, it is, 43 and 44, the next two are together really. Perhaps you would read it out?

A "Smith and colleagues followed a group of about....."

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(quoted).

Q508 Do I take the central point there to be that they only followed up those who were still alive?

A Yes.

Q509 As oral cancer sufferers if there were any you wouldn't expect them to have been --

A They may have been dead. May I comment as well on that. One, they inspected a group of 1500 people. Only 2 to 3 on a very rough calculation, that would put a figure of zero on the very borderline of statistical significance as meaning anything. Zero is always a very attractive figure but statistically it can --

Q510 But personally, have you any comment on that?

A I would wish to read the paper, but certainly I am reading the pains of emanant epidemiologists here.

Q511 Going to Browne, that's at 32, that's going back a bit now, to the second paragraph after Martinez, if you can find that. Can you find that?

A Yes.

Q512 Would you read that for me?

A Page 39, My Lord, at the bottom of page. "Browne et al interviewed....." (quoted).

Q513 Now, and the next one is Wynder and Stellman, note 34 which is, I think, two paragraphs on, second next paragraph?

A "two large case control studies were not...." (Quoted).

Q514 And finally, Winn which is note 42. It's the end of the first paragraph under cohort studies, the second half of that paragraph?

A "In a 16 year follow up...." (quoted).

THE WITNESS THEN WITHDREW.

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